REMARKS

Claims 24-39 are pending in the application. Claims 24, 25, and 35-39 are withdrawn as being directed to non-elected subject matter. Claims 24, 26, 27, 31, 32, and 34 have been amended to further clarify the intended subject matter of the claimed invention. Claims 26, 27, and 31 were amended such that they no longer depend on non-elected claim 24. Claims 24, 26, and 31 have been amended to remove the biologically active fragment embodiment, which allegedly rendered these claims indefinite. Claim 32 was amended as suggested by the Examiner as Applicants intended this claim to depend from claim 31. Claim 34 was amended to clarify the intended scope of the claimed invention and to address the enablement rejection under 35 U.S.C. § 112. These amendments do not introduce new issues, and place the subject application in condition for allowance and/or simplify issues for appeal. Accordingly, entry of the amendments is proper and respectfully requested. Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

Amendment to the Specification

The specification has been amended to correct inadvertent errors. At page 9 of the specification, the identification of the sequences contained in the table, starting at line 27, now corresponds to the sequence listing. Entry of the amendment is respectfully requested.

Objections to the Claims

Claims 26, 27, and 31 were objected to because they depended upon non-elected claim 24. These claims have been amended such that they no longer depend on claim 24. Withdrawal of the objections to these claims is therefore respectfully requested.

Utility Rejections under 35 U.S.C. §101 and §112, First Paragraph

Claims 26-34 have been rejected under 35 U.S.C. §101 and §112, first paragraph, on the grounds that the claimed invention allegedly "is not supported by either a specific and substantial asserted utility or a well established utility" (Final Office Action, page 3). Applicants traverse the

rejections for the reasons already made of record in the Declaration of Dr. Tod Bedilion, the response to the Office Action of September 12, 2002, and on the following grounds

Nothing in the law requires the Applicants to prove biological function, and the Office Action does not point to anything in the law suggesting such a requirement. Indeed, the only law on this point is to the contrary: it is settled law -- and the Office Action does not rebut this -- that how an invention works (that is, its function) is utterly irrelevant to the utility analysis. In short, the entirety of the Office Action's argument is based on the confusion between, and improper equation of, use and function.

The Office Action alleges that the instant specification "lacks any mentioning of toxicology testing" (Final Office Action, page 14). This is untrue. See the specification, for example at page 2, lines 3-10, page 12, lines 24-33, and pages 21-22 for a discussion of toxicology studies, and the use of microarrays for monitoring therapeutics and treatment of disease. For example, the specification recites that "[t]herapeutic efficacy and **toxicity** may be determined by standard pharmaceutical procedures" (page 20, lines 20-21; emphasis added). Also, the specification recites that polynucleotides which encode the claimed polypeptides can be included on a microarray that "can be used to monitor the expression level of large numbers of genes," and this information may be used "to develop and monitor the activities of therapeutic agents" (page 12, lines 24-30). Furthermore, well-established utilities, such as toxicology testing, need not be explicitly disclosed in a patent application. The Declaration of Dr. Tod Bedilion further describes the practical uses of the claimed invention in gene and protein expression monitoring applications as they would have been understood at the time the patent application was filed.

The Bedilion Declaration, at ¶ 10, specifically discusses how the teachings of the Lal '750 application clearly include using differential gene expression analyses in toxicity and drug evaluation studies. In particular, ¶ 10 states that "[t]he Lal '750 application discloses that the polynucleotide sequences disclosed therein, including the SEQ ID NO:1-encoding polynucleotides, are useful as probes in microarrays." It further teaches that the microarrays can be used "to monitor the expression level of large numbers of genes simultaneously" for a number of purposes, including "to develop and monitor the activities of therapeutic agents" (Lal '750 application at p. 66, line 29 through p. 77, line 4)." ¶ 10 goes on to discuss how the Lal '750 application teaches that microarrays can be prepared using the previously mentioned cDNA microarray technology developed at Stanford in the early to mid-1990s, and in particular cites the Schena 1996 (reference (a) of the Bedilion Declaration) as one of a

number of documents that were published prior to the September 23, 1997 filing date of the Lal '750 application that describes the use of the Stanford-developed cDNA technology in a wide range of gene expression monitoring applications, including monitoring and analyzing gene expression patterns in human cancer. Thus the Lal '750 application specifically teaches toxicity testing and drug discovery using the encoding polynucleotides of the invention.

The Examiner further asserts that in order for a polynucleotide to be useful in diagnosis of a disease, there must be a well established or disclosed correlation between the claimed polynucleotide and a disease or disorder (Final Office Action, p. 18). This is not true. Applicants need not demonstrate whether the claimed polynucleotides are associated with disease, only whether the claimed polynucleotides are useful. The claimed polynucleotides are useful whether or not the claimed polynucelotides are associated with disease. Each individual sequence has a utility in creating arrays. Each sequence has a unique and specific utility in that it records the expression level of a unique gene or protein, and can provide information regarding changes in expression in response to a putative therapeutic and/or toxic agent. This is a substantial, "real world" utility in that one of ordinary skill in the art would know how to use the claimed sequences in an array without any further experimentation.

If a drug candidate, targeted to a polynucleotide other than the claimed polynucleotide or targeted to a polypeptide other than the polypeptide encoded by the claimed polynucleotide, alters expression of the claimed polynucleotide, that drug candidate is considered to have an undesirable side effect. As Dr. Bedilion explains in his declaration, good drugs "have strong effects on a specific biological target and minimal effects on all other biological targets" (Bedilion Declaration, ¶ 10). Disruption of the expression of a polynucleotide which is not the target of a drug candidate is, therefore, an undesired side effect of that drug candidate. Measuring the expression level of the claimed polynucleotide, such as during a toxicology test of a drug candidate targeted to another polynucleotide, would **not** require knowledge of the biological function or disease association of the claimed polynucleotide, as the Office Action would have it.

Furthermore, in toxicology testing, every distinct polynucleotide expressed in humans has utility based solely on the property of being expressed in humans. However, the results obtained from using any particular human-expressed polynucleotide in toxicology testing is **specific to both the compound being tested and the polynucleotide used in the test**. No two human-expressed polynucleotides

are interchangeable for toxicology testing because the effects on the expression of any two such polynucleotides will differ depending on the identity of the compound tested and the identities of the two polynucleotides. Therefore, the asserted utility of the claimed polynucleotide for toxicology testing is specific and substantial, and more than adequately satisfies the statutory requirements for utility.

The Office Action's argument amounts to nothing more than the Patent Office's disagreement with the Bedilion Declaration and the Applicants' assertions about the knowledge of a person of ordinary skill in the art, and is tantamount to the substitution of the Patent Office's own judgment for that of the Applicants' expert. The Patent Office is, moreover, wrong on the facts because the Bedilion Declaration demonstrates how one of skill in the art, reading the specification at the time the application was filed, would have understood that specification to disclose the use of SEQ ID NO:2 in gene expression monitoring for toxicology testing, drug development, and the diagnosis of disease (See the Bedilion Declaration at, e.g., ¶¶ 10-16).

The Examiner implies that the references cited and discussed in the Bedilion Declaration have not been properly considered because they were not cited in the specification, nor included in Applicants' information disclosure statement (Final Office Action at page 18). Applicants respectfully submit that a person of ordinary skill in the art is presumed to possess knowledge, not only of the literature made a part of the prosecution record, but also of all relevant literature existing as of the time of Applicants' priority date. Therefore, it is irrelevant whether the documents referred to were first made part of the record at the point when the declaration was submitted, so long as they were available to skilled artisans as of the priority date. However, to expedite prosecution, Applicants have included the references cited in the Bedilion Declaration in a supplemental information disclosure statement submitted concurrently with this response.

For at least the above reasons, withdrawal of the rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112 is respectfully requested.

Written description rejections under 35 U.S.C. § 112, first paragraph

Claims 26, 29-31, 33, and 34 have been rejected under the first paragraph of 35 U.S.C. 112 for alleged lack of an adequate written description. This rejection is respectfully traversed.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first

paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that :

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics[42] which provide evidence that applicant was in possession of the claimed invention,[43] i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.[44] What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.[45] If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.[46]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

SEQ ID NO:1 and SEQ ID NO:2 are specifically disclosed in the application (see, for example, page 2, lines 18-22). Variants of SEQ ID NO:2, including SEQ ID NO: 9-11, are described, for example, at page 9, line 27 through page 10, line 3. Incyte clones in which the nucleic acids encoding the human cancer marker protein were first identified and libraries from which those clones were isolated are described, for example, at page 8, lines 20-25 of the Specification. Chemical and structural features of cancer marker protein are described, for example, on page 8, lines 26-33. Given SEQ ID NO:1 and SEQ ID NO:2, one of ordinary skill in the art would recognize naturally-occurring variants of SEQ ID NO:2 having 90% sequence identity to SEQ ID NO:2 and polynucleotides encoding naturally-occurring variants of SEQ ID NO:1 having 90% sequence identity to SEQ ID NO:1. Accordingly, the Specification provides an adequate written description of the recited polynucleotide sequences.

A. The Specification provides an adequate written description of the claimed variants

and fragments of SEQ ID NO:2.

The Office Action has further asserted that the claims are not supported by an adequate written description because "neither the description of the structure and function of SEQ ID NO:1 and a DNA encoding thereof SEQ ID NO:2 nor the disclosure [sic] solely structural features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus" (Final Office Action, page 9).

Such a position is believed to present a misapplication of the law.

1. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

> 1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

> A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. §112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polynucleotides in terms of chemical structure, rather than on functional characteristics. For example, the "variant language" of independent claims 26 and 33 recite chemical structure to define the claimed genus:

> 26. An isolated polynucleotide encoding a polypeptide selected from the group consisting of: ... b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1...
>
> 33. An isolated polynucleotide selected from the group consisting of: ...b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to a polynucleotide sequence of SEQ ID NO:2...

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:1 and SEQ ID NO:2. In the present case, there is no reliance merely on a description of functional characteristics of the polynucleotides recited by the claims. In fact, there is no recitation of functional characteristics. Moreover, if such functional recitations were included, it would add to the structural characterization of the recited polynucleotides. The polynucleotides defined in the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type. By failing to base its written description inquiry "on whatever is now claimed," the Office Action failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in

Lilly and *Fiers*

2. The present claims do not define a genus which is "highly variant"

Furthermore, the claims at issue do not describe a genus which could be characterized as "highly variant." Available evidence illustrates that the claimed genus is of narrow scope.

In support of this assertion, the Examiner's attention is directed to the enclosed reference by Brenner et al. ("Assessing sequence comparison methods with reliable structurally identified distant evolutionary relationships," Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078). Through exhaustive analysis of a data set of proteins with known structural and functional relationships and with <90% overall sequence identity, Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. (Brenner et al., pages 6073 and 6076.) Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins. (Brenner et al., page 6076.)

The present application is directed, *inter alia*, to cancer marker proteins related to the amino acid sequence of SEQ ID NO:2. In accordance with Brenner et al, naturally occurring molecules may exist which could be characterized as cancer marker proteins and which have as little as 40% identity over at least 70 residues to SEQ ID NO:2. The "variant language" of the present claims recites, for example, polynucleotides encoding "a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1" (note that SEQ ID NO:1 has 340 amino acid residues). This variation is far less than that of all potential cancer marker proteins related to SEQ ID NO:1, i.e., those cancer marker proteins having as little as 40% identity over at least 70 residues to SEQ ID NO:1.

3. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. §112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written description inquiry in those case was

based on the state of the art at essentially at the "dark ages" of recombinant DNA technology.

The present application has a priority date of September 23, 1997. Much has happened in the development of recombinant DNA technology in the 20 or more years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances one of skill in the art would recognize that, given the sequence information of SEQ ID NO:1 and SEQ ID NO:2, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polynucleotide variants at the time of filing of this application.

4. Summary

The Office Action failed to base its written description inquiry "on whatever is now claimed." Consequently, the Action did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:1 or SEQ ID NO:2. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polynucleotides defined by the present claims is adequately described, as evidenced by Brenner et al and consideration of the claims of the '740 patent involved in *Lilly*. Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Office Action.

Enablement rejections under 35 U.S.C. § 112, first paragraph

Claim 33 is rejected for allegedly failing to meet the requirements of 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not provide an enabling disclosure commensurate in scope with the claims (Final Office Action page 10). In particular, the Examiner alleges that the specification "does not reasonably provide enablement for a DNA comprising at least 60 nucleotides of

SEQ ID NO:2 or a sequence that is 90% identical thereto" and that "the specification does not establish... regions of the protein structure which may be modified without effecting [sic] the specific requisite activity of the polypeptide of the instant invention" (Final Office Action, page 11). Applicants traverse the rejection for at least the following reasons.

As a preliminary matter, Applicants have construed the rejection to include claim 34. Claim 34 has been amended to recite "[a]n isolated polynucleotide consisting of 60 contiguous nucleotides of a polynucleotide of claim 33." This amendment clarifies the intended scope of claim 34. Applicants have construed the rejection to include claim 34.

The first paragraph of 35 U.S.C. §112 requires that the Specification describe how to make and use the claimed subject matter. As set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be take as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Applicants submit that the disclosure amply enables the claimed invention. Note that claim 33, for example, recites not only that the polynucleotides have a sequence that is at least 90% identical to SEQ ID NO:2, but also that they have "**a naturally occurring polynucleotide sequence**." Through the process of natural selection, nature will have determined the appropriate polynucleotide sequences. Given the information provided by SEQ ID NO:2, one of skill in the art would be able to routinely obtain "a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to a polynucleotide sequence of SEQ ID NO:2." For example, the identification of relevant polynucleotides could be performed by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed and/or described throughout the Specification of the instant application. See, e.g., page 11, line 21 through page 12, line 23; and Example VII at pages 28-32. Thus, one skilled in the art need not make and test vast numbers of

polynucleotides. Instead, one skilled in the art need only screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides that already exist in nature.

The specification also describes the expression vectors into which the claimed fragments could be inserted, and the construction of fusion proteins (pages 13-14, page 36, lines 19-30, and page 37, lines 14-20). Given this guidance, one of ordinary skill in the art would readily understand how to select and screen polynucleotides encoding fragments of SEQ ID NO:1 without any undue experimentation.

Applicants respectfully point out that the claims are directed to polynucleotides, not polypeptides, and it is the functionality of the claimed polynucleotides, not the polypeptides encoded by them, that is relevant. Members of the claimed genus of variants may include, for example, mutant alleles associated with diseases, or single nucleotide polymorphisms (SNPs). Members of the claimed genus of variants may be useful even if they encode defective polypeptides. For example, the variant polynucleotides could be used for the detection of sequences related to cancer marker protein (see the specification a page 6, lines 16-19, and page 10, lines 11) including variants that may be associated with disease states, such as the diseases listed on page 6, lines 11-15, of the specification. See the specification at, for example, pages 16-17 for disclosure of how to use the claimed sequences in diagnostic assays.

Since the claims of the instant application are drawn to naturally-occurring variants, it is not necessary to screen every conceivable variant which might be made using recombinant methods, as all that is claimed are those variant sequences which are found in nature. Given the sequences of SEQ ID NO:1 and SEQ ID NO:2, one of ordinary skill in the art could readily identify naturally occurring polynucleotides having 90% identity to SEQ ID NO:2 and polynucleotides encoding a polypeptide having at least 90% identity to SEQ ID NO:1, using well known methods of sequence analysis, without any undue experimentation. The skilled artisan would also know how to use the claimed polynucleotides, for example in expression profiling, disease diagnosis, or detection of related sequences as discussed above.

For at least the above reasons, withdrawal of the enablement rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 26 and dependent claims 29-32 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." (Final Office Action, page 13).

Claim 24, 26, and 31 have been amended to remove the biologically active fragment embodiment, which allegedly rendered these claims indefinite. Therefore, the rejections with respect to these claims are moot.

Claim 32 was amended as suggested by the Examiner as Applicants intended this claim to depend from claim 31.

For at least the above reasons, Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections and rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney/Agent below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108**, as set forth in the enclosed fee transmittal letter.

Respectfully submitted,
INCYTE CORPORATION

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

The paragraph beginning at page 9, line 27, has been replaced with the following rewritten paragraph:

Mammalian variants of the cDNA encoding cancer marker protein were identified using BLAST2 with default parameters and the ZOOSEQ databases (Incyte Genomics). These preferred variants have about 90% identity to the human protein as shown in the table below. The first column shows the SEQ ID_H for the human cDNA; the second column, the SEQ ID_{VAR} for variant cDNAs; the third column, the clone numbers for the variants; the fourth column, the percent identity to the human cDNA; and the fifth column, the nucleotide alignment (Nt_H) of the human and variant cDNAs.

SEQ ID_H	SEQ ID_{VAR}	Clone No.	Identity	Nt_H Alignment
1	[10] 9	[008031_Cf.1] 70275863	89%	541-1123
1	[1] 10	034237_Mm.1	90%	667-1173
1	[12] 11	702482342	89%	671-1173

IN THE CLAIMS:

Claims 24, 26, 27, 31, 32, and 34 have been amended as follows:

24. (Once Amended) An isolated polypeptide selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence of SEQ ID NO:1,

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1,

[c) a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:1,] and

[d)] c) an immunogenic fragment of a polypeptide having an amino acid sequence of SEQ ID NO:1.

26. (Once Amended) An isolated polynucleotide encoding a polypeptide [of claim 24] selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence of SEQ ID NO:1,

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1,

c) an immunogenic fragment of a polypeptide consisting of an amino acid sequence of SEQ ID NO:1.

27. (Once Amended) An isolated polynucleotide encoding a polypeptide [of claim 25] comprising an amino acid sequence of SEQ ID NO:1.

31. (Once Amended) A method of producing a polypeptide [of claim 24] selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence of SEQ ID NO:1,

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1, and

c) an immunogenic fragment of a polypeptide consisting of an amino acid sequence of SEQ ID NO:1.,

the method comprising:

[a)] 1) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide of claim 26 [encoding the polypeptide of claim 24], and

[b)] 2) recovering the polypeptide so expressed.

32. (Once Amended) A method of claim [9] 31, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO:1.

34. (Once Amended) An isolated polynucleotide [comprising at least] consisting of 60 contiguous nucleotides of a polynucleotide of claim 33.